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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
| 08/473,789 | 06/07/95 | CURTISS | R MEGAN-100-21 |
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| RYAN V ART UNIT | PAPER NUMBER |
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1641

DATE MAILED:

06/14/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 3/18/99

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-32, 35-40 is/are pending in the application.
Of the above, claim(s) 5-7, 15, 17-19, 21, 22, 25, 26, 36, 38 is/are withdrawn from consideration.
☒ Claim(s) 9 is/are allowed.
☒ Claim(s) 1-4, 8, 10-14, 16, 20, 23, 24, 27-32, 35, 37, 39, 40 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.
☐ received in Application No. (Series Code/Serial Number) _____
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

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DETAILED ACTION

The text of those sections of U.S. Code not included in this Office Action can be found in a prior Office Action.

The Examiner acknowledges receipt of the amendment filed March 18, 1999.

Election/Restriction

Applicant notes that the Office Action of December 23, 1997 indicates the withdrawal of claims 30-35 from consideration by the Examiner. Since the Office Action of April 15, 1997 rejoined claims 30-35 to the elected invention, these claims (i.e., claims 30-32 and 35) will be included in the claims now under examination.

In this application:

Claims 33 and 34 were canceled.

Claims 39 and 40 were added.

Claims 1-32 and 35-40 are now pending.

Claims 5-7, 15, 17-19, 21, 22, 25, 26, 36 and 38 are withdrawn from consideration.

Claims 1-4, 8-14, 16, 20, 23, 24, 27-32, 35, 37, 39 and 40 are now under examination.

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Response to Amendment

Applicant's arguments filed March 18, 1999 have been fully considered and they are not deemed to be persuasive regarding those rejections which are maintained.

(1) The rejection of claims 1-5, 8-14, 16, 20, 23, 24, 27-29 and 37 under 35 U.S.C. 112, second paragraph is withdrawn.

(2) The rejection of claims 1-5, 8, 10-14, 16, 20, 23, 24, 27-29, and 37 under 35 U.S.C. 102(e) as being anticipated by Szafranski et al is withdrawn.

(3) The rejection of claims 1-4, 8, 10-14, 16, 20, 23, 24, 27-29 and 37 (and now claims 30-32 and 35) under 35 U.S.C. 102(e) as being anticipated by Molin et al is maintained. The rejection of claim 9 is withdrawn. Claim 5 is not included in this rejection.

Applicant asserts that Molin et al fail to disclose the use of environmentally regulated essential gene that is expressed under conditions where the lethal gene is not, and not expressed under conditions where the lethal gene is expressed.

Molin et al disclose a biological containment system comprised of suicide genes, such as the hok gene, and an essential gene, such as the sok gene. Molin et al also disclose the activity of sok depends on the presence of one or more specific environmental factors, such as body temperature. When

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the factors are not present, the promoter will become inactive thereby causing the suppression of the sok gene and expression of the hok (lethal) gene. (See especially column 6, lines 24-46; column 11, lines 14-25; column 16, lines 64-67)

(4) The rejection of claims 1, 2, 4, 8-14, 16, 20, 27-28, and 37 under 35 U.S.C. 112, first paragraph is withdrawn; however, the rejection of claims 3, 23, 24, 29-32, and 35 is maintained.

Applicant maintains that the claimed invention is not a bacterial attenuation system, but results in the viability of the cell in a permissive environment and non-viability in a non-permissive environment.

The claims are directed to a microbial cell which is viable in a permissive environment (i.e., inside a warm-blooded animal). The claims, therefore, can be interpreted as administering live virulent microorganisms to an animal host. Molin et al, however, teaches that the use of live vaccines has been limited because "it is often difficult to obtain the right combination of attenuation, viability and relevant immune response." (See column 13).

The specification does not teach how to use bacteria such as *Yersinia pestis* or *Moraxella catarrhalis*, for example, as vaccine compositions. Furthermore, there are no known vaccines for these

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diseases. In view of the absence of working examples, the breadth of the claims, and the unpredictable state of the art, it would require undue experimentation for one skilled in the art to practice the entire scope of the claimed invention.

(5) The rejection of claims 1-3, 10-12, 23, 27, and 28 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (Proc. Natl. Acad. Sci) is maintained; however, the rejection of claims 13, 16, 20, 24 and 37 is withdrawn.

In response to the rejection based on the reference of Gerdes et al (Proc. Natl. Acad. Sci), Applicant submits that the references discloses *E. coli* containing a hok gene linked to a lambda PR which is regulated by the temperature-sensitive lambda CI857 repressor. However, Applicant asserts the sok gene is not an environmentally regulated essential gene, but a regulatory gene since it is not essential to the viability of the cell.

Gerdes et al teach a plasmid comprised of hok and sok gene. The hok gene encodes a toxic product which kills the cell. The sok gene suppresses the cell killing. Therefore, the sok gene is viewed as being essential to the viability of the cell. Furthermore, the reference also teaches the expression of the sok gene at 42 degrees C. (See especially page 3119, second column)

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(6) The rejection of claims 1-3, 10-12, 27, 28, and 37 under 35 U.S.C. 102(b) as being anticipated by Gerdes et al (EMBO Journal) is maintained; however, the rejection of claims 8, 13, 14, 16, 20, and 24 is withdrawn.

Applicant asserts that Gerdes et al teach the hok gene which can be considered a lethal gene but fails to disclose a temperature regulated sok gene.

Gerdes et al teach the sok gene which suppresses the hok gene. Therefore, the sok gene is considered "essential" to the viability of the cell.

The following are new grounds of rejection:

Claim Rejections - 35 USC § 112

Claims 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 39 recites the limitation "the essential gene does not encode a trans regulatory element for the lethal gene". The specification as originally filed does not appear to support this limitation. Applicant refers to page 19, lines 3-5 of the

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specification and defines the trans regulatory element as "a molecule or complex that modulates the expression of a gene". However, although the specification defines the term, the specification does not teach or suggest the negative limitation of "the essential gene does not encode a trans regulatory element for the lethal gene".

Similarly, claim 40 recites the limitation "the essential gene does not regulate expression of the lethal gene". Applicant refers to page 31, lines 27 through page 32, line 4. The specification does not appear to provide support for this limitation.

The Group and/or Art Unit location of your application in the Patent and Trademark Office may have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1641.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to V. Ryan whose telephone number is (703)305-6558.


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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Papers related to this application may be submitted to the Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Art Unit 1641 is (703)308-4242.

V. Ryan
Patent Examiner/Art Unit 1641
June 1999
Ryan/vr


JAMES C. HOUSEL 6/11/99
SUPERVISORY PATENT EXAMINER